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PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,273	THOMAS ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *2,4-6,8,9,18-20,24,25 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7,10-17,21-23 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/15/2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 1, 3, 7, 10-17 and 21-22, drawn to a method of producing a transformed plant by transforming a plant with a chimaeric gene comprising a promoter operably linked to a coding sequence as set forth in SEQ ID NO:2, is acknowledged. The traversal is on the ground(s) that the classification of subject matter of Groups I, II, III and IV is improper because the methods of claims 4 and 5 recite subunit fragments of the same protein claimed in claim 3. Applicant also points to the sequence listing as showing the relatedness of the sequences of Groups I, II, III and IV, and maintains that on the basis of this relatedness the inventions of Groups I-III and IV are not independent. Applicant additionally argues that claims 23 and 26 are improperly classified in Group VI, and points out that a search of sequences encoding RIPs used in claims 1-4 would necessarily search the sequences of claims 23 and 26. Applicant additionally points out that the inventions of Groups I-IV rely on essentially the same function(s) resulting in essentially the same effect. Applicant also argues that a search of the inventions of Groups I-IV and VI would not impose a serious burden. Applicant further requests that claims 1-17, 21-23 and 26 be grouped together, or alternatively that Groups I, II, III and IV be examined together.

This is not found persuasive first because the classification of subject matter of Groups I, II, III, IV and VI is not improper because the classification set forth in the restriction requirement is both exemplary and appropriate to the claimed subject matter. Furthermore, classification is not the sole basis on which the instant restriction requirement was made. The methods of Groups

I, II, III and IV are distinct methods regardless of their classification, as each method requires the use of a specific nucleotide sequence. This is not found persuasive secondly because although sequences used in the methods are related in that they comprise all or a part of a sequence encoding a maize ribosome inactivating protein (SEQ ID NO:1), the sequences differ from each other in structure of the nucleotide sequences used, in the structure, nature and level of activity of the expressed protein, and in their effect upon expression in transgenic plants, and thus require a separate search. In particular, the elected Group II, directed to the use of SEQ ID NO:2, utilizes a sequence which lacks internal as well as C-terminal and N-terminal sequences that are present in SEQ ID NO:1. For this reason a search of the inventions of Groups I-IV would impose a serious burden. However, because the DNA constructs of claims 23 and 26 are not directed to any particular sequence and recite claim language recited in the broad claims examined in Group II, claims 23 and 26 of Group VI are also examined herein, in addition to claims 1, 3, 7, 10-17 and 21-22 of Group II. Claims 2, 4-6, 8-9, 18-20, 24-25 and 27 are withdrawn from consideration as being directed to nonelected inventions.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed September 10, 2002, is attached to the instant Office action.

Claim Objections

Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 7 is directed to a method according to claims 1 or 3 that requires the use of a coding sequence identified in SEQ ID NO:2 or a coding sequence which is homologous thereto. Claim 1 is directed to a method that requires the use of a coding sequence which encodes a maize ribosome inactivating protein or a part thereof. The limitation "a coding sequence which is homologous thereto" in claim 7 does not further limit "a coding sequence which encodes a maize ribosome inactivating protein or a part thereof" in claim 1.

Claims 10-17, 21 and 22 are objected to because of the following informalities: the claims depend from nonelected claims. Appropriate correction is required.

Claims 10-13 are objected to because of the following informalities: the claims recite sequence identifiers of nonelected inventions. Appropriate correction is required.

Claims 10-17 and 21-22 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). For examination purposes the claims are interpreted as depending from the elected claim of the lowest numerical value.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 7, 10-17, 21-23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of producing a transgenic plant transformed with a chimaeric gene comprising a coding sequence, including SEQ ID NO:2 or a sequence homologous thereto and including sequences having 70-90% homology to SEQ ID NO:2, encoding a maize ribosome inactivating protein or a part thereof, the expression of which causes plant cytotoxicity at a target site. The claims are further drawn to a transgenic plant cell or plant produced by said method, and to a DNA isolate and expression vehicle.

The specification describes a single maize Type 3 ribosome inactivating protein that is synthesized as a single polypeptide chain (maize pro-RIP) comprising two active peptide domains, the α domain and the β domain, separated by a central peptide spacer and flanked by N and C terminal peptides (page 6 lines 6-19). The specification also describes SEQ ID NO:1 as comprising the maize pro-RIP coding sequence, SEQ ID NOS: 3 and 4 as comprising the α domain and the β domain coding sequences respectively, and the elected sequence of SEQ ID NO:2 as a recombinant mature RIP (RIP-P) comprising the α domain and the β domain arranged contiguously, without the central peptide spacer and without the N and C terminal peptides (page 8 line 4 to page 10 line 4). The specification additionally describes the α domain coding sequence and the recombinant mature RIP (RIP-P) coding sequence as causing plant cytotoxicity

when expressed alone, and the α domain coding sequence and the β domain coding sequences as causing plant cytotoxicity when co-expressed (pages 23-26).

In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus, nor the structural features unique to the genus. The specification does not describe ribosome inactivating proteins other than type 3 ribosome inactivating proteins obtained from maize, or the nucleic acid sequences encoding them, although the specification does indicate that three distinct types of plant ribosome inactivating proteins (types 1-3) that differ in their structural and functional properties have been described in the prior art (pages 5-6). The prior art also indicates that maize harbors two species of only one type of ribosome inactivating protein, the type 3 ribosome inactivating protein (Bass et al., Plant Physiology, 1995, Vol. 107, pages 661-662, Applicant's IDS), yet claims 1, 23 and 26 are directed to any maize ribosome inactivating protein without reference to its specific structural or functional characteristics. Further, while the specification indicates that only specific parts of a maize ribosome inactivating protein cause cytotoxicity when expressed, the rejected claims are directed to any part of a maize ribosome inactivating protein. Additionally, the specification does not describe the structure of sequences characterized as being evolutionarily related (homologous) to SEQ ID NO:2, or sequences specifically having 70-90% homology to SEQ ID NO:2, that encode functional proteins.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members

of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Claims 1, 3, 7, 10-17, 21-23 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a transgenic Solanaceous plant transformed with a chimaeric gene comprising a coding sequence of SEQ ID NO:2 encoding a recombinant mature maize ribosome inactivating protein comprising an α domain and a β domain arranged contiguously, the expression of which inactivates the plant's ribosomes, does not reasonably provide enablement for a method of producing a transgenic plant of any species transformed with a chimaeric gene comprising a coding sequence have any unspecified type of homology to SEQ ID NO:2 or having 70-90% homology to SEQ ID NO:2 or encoding any unidentified maize ribosome inactivating protein or any undefined part thereof, the expression of which causes any unidentified type of plant cytotoxicity at any unspecified target site. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a method of producing a transgenic plant transformed with a chimaeric gene comprising a promoter which is induced at, and or adjacent to, a target site, said promoter operably linked to a coding sequence, including SEQ ID NO:2 or a sequence homologous thereto and including sequences having 70-90% homology to SEQ ID NO:2, encoding a maize ribosome inactivating protein or a part thereof, the expression of which causes plant cytotoxicity at a target site. The claims are also drawn to a transgenic plant cell or plant

produced by said method, and to a DNA isolate and expression vehicle. The claims are further drawn to the use of transcriptional or translational enhancer sequences and/or intracellular targeting sequences and introns, and/or nucleotide sequences operable to facilitate the transformation process and stable expression of the chimaeric gene.

The specification discloses the transformation of tobacco and potato plants with chimaeric genes corresponding to a maize type 3 ribosome inactivating protein, including chimaeric genes comprising the elected sequence of SEQ ID NO:2 encoding a recombinant mature RIP (RIP-P) comprising the α domain and the β domain of the maize ribosome inactivating protein arranged contiguously, without the central peptide spacer and without the N and C terminal peptides (pages 20-50). The specification specifically discloses that expression of SEQ ID NO:2 operably linked to a constitutive promoter in transgenic tobacco cell protoplasts inactivates ribosomes located both in the cytosol and on the endoplasmic reticulum (pages 23-25), that transgenic potato plants expressing SEQ ID NO:2 from a nematode responsive promoter exhibit reduced susceptibility to nematodes as compared to nontransformed control plants (page 41), and that transgenic potato plants expressing SEQ ID NO:2 from a tapetal specific promoter exhibit male sterility as compared to nontransformed control plants (pages 44-50).

The specification does not disclose maize ribosome inactivating proteins other than the type 3 maize ribosome inactivating protein encoded by SEQ ID NO:1. The specification also does not disclose transformation of plants with chimaeric genes comprising functional parts of the maize ribosome inactivating protein other than the α domain, which can function independently, or the β domain, which functions only in the presence of the α domain. Additionally, the specification does not disclose sequences characterized as being evolutionarily

related (homologous) to SEQ ID NO:2, or sequences specifically having 70-90% homology to SEQ ID NO:2 that encode functional proteins. Furthermore, the specification does not disclose the effect of expressing a maize ribosome inactivating protein in plants other than Solanaceous plants, or plant cytotoxic effects other than ribosome inactivation. Finally, the specification does not disclose transcriptional or translational enhancer sequences and/or intracellular targeting sequences and introns, and/or nucleotide sequences operable to facilitate the transformation process and stable expression of the chimaeric gene.

The specification does not enable methods of producing transgenic plants transformed with chimaeric genes encoding maize ribosome inactivating proteins other than type 3 ribosome inactivating proteins, as maize ribosome inactivating proteins other than type 3 ribosome inactivating proteins are not disclosed or known in the art. In the absence of further guidance, undue experimentation would be required by one skilled in the art to identify and isolate coding sequences for other types of maize ribosome inactivating proteins that would cause plant cytotoxicity at a target site in the same manner as the maize type 3 ribosome inactivating protein exemplified.

The specification also does not enable methods of producing transgenic plants transformed with chimaeric genes encoding maize ribosome inactivating protein parts other than the α domain alone, or the β domain in combination with the α domain, as functional type 3 ribosome inactivating protein parts other than the α domain alone, or the β domain in combination with the α domain, are not disclosed or known in the art. In the absence of further guidance, undue experimentation would be required by one skilled in the art to identify and

characterize other type 3 ribosome inactivating protein parts that would cause plant cytotoxicity at a target site in the same manner as maize ribosome inactivating protein parts exemplified.

The specification additionally does not provide sufficient guidance for one skilled in the art to make and/or use the full scope of the claimed invention without undue experimentation because the effect of expressing a chimaeric gene comprising a coding sequence have any unspecified type of homology to SEQ ID NO:2 or having 70-90% homology to SEQ ID NO:2 or encoding any unidentified maize ribosome inactivating protein or any undefined part thereof is unpredictable. The effect is unpredictable because even though different ribosome inactivating proteins share structurally similar regions, they vary in their ability to inactivate ribosomes. See for example Stirpe et al. (Biotechnology, 1992, Vol. 10, pages 405-412, Applicant's IDS), teaching that the effect of ribosome inactivating proteins on plant ribosomes is variable, and that each particular ribosome inactivating protein has its own specific pattern of activity on ribosomes from organisms belonging to different genera (page 408 column 1). In the instant case Applicant has not provided guidance concerning how to distinguish between those sequences that would have the desired effect upon expression in a transgenic plant and those that would not, as the effect of expressing only a single type of ribosome inactivating protein obtained from a single species of plant is exemplified.

The specification also does not provide sufficient guidance for one skilled in the art to make and/or use the full scope of the claimed invention without undue experimentation because the effect of expressing a chimaeric gene comprising a coding sequence of SEQ ID NO:2 in a wide variety of different plant species is unpredictable. The effect is unpredictable because plant ribosomes from different plant species exhibit different levels of susceptibility to different

ribosome inactivating proteins. See for example Stirpe et al. (Biotechnology, 1992, Vol. 10, pages 405-412, Applicant's IDS), teaching that the effect of ribosome inactivating proteins on plant ribosomes is variable, and that ribosomes from an organism belonging to a particular species has a specific spectrum of sensitivity to different ribosome inactivating proteins (page 408 column 1). See also Hey et al. (Plant Physiology, 1995, 107:1323-1332), teaching that tobacco ribosomes are susceptible to inactivation by the active form of maize ribosome inactivating protein, whereas maize ribosomes are resistant (page 1330 column 1). In the instant case Applicant has not provided guidance concerning which non-Solanaceous plant ribosomes would be susceptible to inactivation by the protein encoded by SEQ ID NO:2, as only effects on Solanaceous plants are exemplified.

The specification further does not provide sufficient guidance for one skilled in the art to make and/or use the full scope of the claimed invention without undue experimentation because the ability of a chimaeric gene comprising a coding sequence of SEQ ID NO:2 to produce plant cytotoxic effects other than ribosome inactivation upon expression is unpredictable. Plant cells can be subject to cytotoxic effects that involve a variety of different cellular structures and processes and that are mediated by a variety of different mechanisms. See for example Czako et al. (Plant Physiology, 1994, 104:1067-1071), teaching cytotoxic effects that occur in the nucleus as a consequence of phosphorylating nucleotide analogs and inhibiting DNA replication by expressing in plant cells a chimaeric gene comprising a coding sequence for the HSVtk gene, O'Keefe et al. (Plant Physiology, 1994, 105:473-482,) teaching cytotoxic effects that occur in plastids as a consequence of N-dealkylating of R7402 and inhibiting protein synthesis by expressing in plant cells a chimaeric gene comprising a coding sequence for the $P450_{SU1}$ gene,

and Tsugeki et al. (PNAS October 26, 1999, Vol. 96, No. 22, pages 12941-12946), teaching cytotoxic effects that occur in the cytosol as a consequence of ribosylating the E2F translation initiation factor and inhibiting protein synthesis by expressing in plant cells a chimaeric gene comprising a coding sequence for the $P450_{SU1}$ gene. In the instant case Applicant has not provided guidance concerning which cytotoxic effects other than ribosome inactivation to screen for, as only methods for determining the effect of expressing SEQ ID NO:2 on ribosome inactivation are disclosed.

Finally, the specification does not enable methods of producing transgenic plants transformed with chimaeric genes further comprising transcriptional or translational enhancer sequences and/or intracellular targeting sequences and introns, and/or nucleotide sequences operable to facilitate the transformation process and stable expression of the chimaeric gene, as the specification provides no guidance with respect to which specific additional sequences to use or in what combination. In the absence of further guidance, undue experimentation would be required by one skilled in the art to select from among the numerous diverse sequences available those particular sequences that, when included as part of a chimaeric gene encoding a maize ribosome inactivating protein, would function in concert with the chimaeric gene to cause plant cytotoxicity at a target site in the same manner as the chimaeric gene exemplified.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 10-13, 16, 21, 22, 23 and 26, and claims 3, 7, and 14-17 dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 21, 22, 23 and 26, and claims dependent thereon, are indefinite in the recitation of "target site". It is unclear from the claim language what "target site" refers to, as "target site" could be interpreted in more than one way in light of Applicant's disclosure. For example, "target site" could be interpreted as a location in the plant body (root, flower, stem, etc.) or in a plant cell (nucleus) where expression of the sequence encoding a maize ribosome inactivating protein occurs. Alternatively, "target site" could be interpreted as the specific intracellular location at which the maize ribosome inactivating protein effects cytotoxicity, e.g. the ribosome.

Claims 1, 21, 22, 23 and 26, and claims dependent thereon, are indefinite in the recitation of "which promoter is induced at and/or adjacent to a target site". First, it is unclear how induction of the promoter "adjacent to" a target site would cause cytotoxicity, as claim 1 also recites that the expression of the gene causes cytotoxicity "at" a target site. Second, it is unclear where or under what circumstances the promoter is induced, because, as discussed *supra*, the meaning of "target site" is unclear. For example, if "target site" refers to a specific intracellular location at which the maize ribosome inactivating protein effects cytotoxicity, it is unclear how the promoter could be induced at and/or adjacent to this particular site, as the maize ribosome inactivating protein effects cytotoxicity at the ribosome, but promoter induction would occur in the nucleus.

Claims 11-13, and claims dependent thereon, are indefinite in the recitation of "% homology with". It is unclear in what way the sequences have "% homology" with each other, as

"homology" may interpreted in more than one way, such as structural homology, or functional homology.

Claim 10, and claims dependent thereon, are indefinite in the recitation of "has at least 70% with ...". It is unclear what "70%" refers to, as "70%" does not modify any quantifiable characteristic recited in the claim.

Claim 16 is indefinite in the recitation of "selected from the group comprising". The using of the term "comprising" in this context is indefinite. The term "comprising" does not define the metes and bounds of a closed group, as "comprising" is open claim language that would encompass all 3' untranslated terminator sequences in addition to those specifically recited. It is suggested that the claim be amended to recite "consisting of" rather than "comprising" in order to overcome the rejection.

Claim 22 is indefinite in the recitation of "plant cell transformed with a chimaeric gene according to the method of any one of claims 1-20". There is insufficient antecedent basis for "plant cell" in claims 1-20, as the methods of claims 1-20 require transformation of "a plant". In order to overcome the rejection, it is suggested that the claim be amended to indicate that the plant cell is obtained from a transgenic plant produced by the claimed method.

Claim 23 is indefinite in the recitation of "a DNA isolate of a chimaeric gene". It is unclear what is intended by this phrase, as the claim makes no reference to what part of the chimaeric gene would be in the isolate, and "DNA isolate of a chimaeric gene" is not explicitly defined in the specification.

Claim 26 is indefinite in the recitation of "biologically functional expression vehicle". It is unclear what is intended by the term "vehicle", as the claim makes no reference to the

structure of the vehicle, or the specific biological function it performs, and "biologically functional expression vehicle" is not explicitly defined in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7, 10, 11-17, 21-23 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Maddaloni et al. (Transgenic Research, 1997, Vol. 6, No. 6, pages 393-402).

The claims are drawn to a method of producing a transgenic plant transformed with a chimaeric gene comprising a promoter which is induced at, and or adjacent to, a target site, said promoter operably linked to a coding sequence, including SEQ ID NO:2 or a sequence homologous thereto and including sequences having 70-90% homology to SEQ ID NO:2, encoding a maize ribosome inactivating protein or a part thereof, the expression of which causes plant cytotoxicity at a target site. The claims are also drawn to said method where the chimaeric gene further comprises a 3' untranslated terminator sequence, including a plant 3' untranslated terminator sequence and including a 3' untranslated terminator sequence selected from the group comprising the pea rbcS E9 terminator sequence, the nos terminator sequence derived from the nopaline synthase gene of Agrobacterium tumefaciens, and the 35S terminator sequence from cauliflower mosaic virus, and to said method where the chimaeric gene comprises nucleotide sequences operable to facilitate the transformation process and the stable expression of said

chimaeric gene. The claims are further drawn to a transgenic plant cell or plant produced by said method, and to a DNA isolate and expression vehicle.

Maddaloni et al. teach a method of producing a transgenic tobacco plant transformed with a chimaeric gene comprising a potato wound-inducible wun1 promoter operably linked to a coding sequence encoding a maize ribosome inactivating protein (page 394 column 1 first column last paragraph; page 396 Figure 1). The potato wun1 promoter is induced by wounding at, and or adjacent to, a wounding target site (paragraph spanning pages 394-395; page 397 Figure 3). The coding sequence taught by Maddaloni et al. is homologous to SEQ ID NO:2 in that it comprises the α and β domains of the maize ribosome inactivating protein of SEQ ID NO:2, although not contiguously. The coding sequence taught by Maddaloni et al. would also have 70-90% homology to SEQ ID NO:2 because it comprises the α and β domains of the maize ribosome inactivating protein of SEQ ID NO:2, and because the claims do not indicate on what basis the sequences are homologous. The expression of the coding sequence taught by Maddaloni et al. would inherently cause plant cytotoxicity at a target site because the maize ribosome inactivating protein has the inherent ability to inactivate heterologous plant ribosomes, including tobacco ribosomes. Maddaloni et al. also teach that their chimaeric gene further comprises a plant 3' untranslated terminator sequence (page 396 Figure 1), and the chimaeric gene taught by Maddaloni et al. comprises nucleotide sequences operable to facilitate the transformation process and the stable expression of said chimaeric gene, as evidenced by their success transformation of tobacco plants and subsequent confirmation of the expression of the maize ribosome inactivating protein. Furthermore, while Maddaloni et al. do not teach the pea rbcS E9 terminator sequence, the nos terminator sequence derived from the nopaline synthase

gene of Agrobacterium tumefaciens, or the 35S terminator sequence from cauliflower mosaic virus, the reference need not teach any of these specific terminator sequences, as claim 16 requires only that the terminator be selected from the group comprising these specific terminator sequences. Since comprising is open language, any terminator sequence used would anticipate the terminator sequence of claim 16.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3 and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maddaloni et al. (Transgenic Research, 1997, Vol. 6, No. 6, pages 393-402) in view of Hey et al. (Plant Physiology, 1995, Vol. 107, pages 1323-1332) and Boston et al. (US 5,332,808 issued July 26, 1994, Applicant's IDS).

Claims 1 and 14-17 are discussed *supra*. Claim 3 is drawn to a method of producing a transgenic plant transformed with a chimaeric gene comprising a promoter which is induced at, and or adjacent to, a target site, said promoter operably linked to a coding sequence comprising a recombinant mature maize RIP comprising an α domain and a β domain arranged contiguously, the expression of which causes plant cytotoxicity at a target site.

The teachings of Maddaloni et al. are discussed *supra*.

Maddaloni et al. do not teach a recombinant mature maize RIP comprising an α domain and a β domain arranged contiguously, or the use of a pea rbcS E9 terminator, a nos terminator, or a CaMV 35S terminator.

Hey et al. teach a biologically active recombinant mature maize RIP comprising an α domain and a β domain arranged contiguously (page 1329 Figure 6 and Table 1).

Boston et al. teach the use of a nos terminator in a plant expression construct designed to express a sequence encoding a maize ribosome activating protein (column 5 lines 65-66).

Given the success of Maddaloni et al. in producing a transgenic plant transformed with a chimaeric gene encoding a maize ribosome inactivating protein, and given the teachings of Hey et al. that a recombinant mature maize RIP comprising an α domain and a β domain arranged contiguously is biologically active, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to substitute the sequence encoding a recombinant mature maize RIP comprising an α domain and a β domain arranged contiguously of Hey et al. for the sequence encoding a maize ribosome inactivating protein for the purpose of producing transgenic plants without any surprising or unexplained results. Additionally, given that the use of the nos terminator in plant transformation constructs was well established at the time of filling, and given the suggestion of Boston et al. to use a nos terminator in a plant expression construct designed to express a sequence encoding a maize ribosome activating protein, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to use a nos terminator in an expression construct comprising a sequence encoding a recombinant mature maize RIP comprising an α domain and a β domain arranged contiguously. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable

expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
December 9, 2003

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER